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The Mercury Contamination in Fish and the Subsequent Public Health Effects

Ashley Spooner
Regis University

THE MERCURY CONTAMINATION IN FISH AND THE SUBSEQUENT PUBLIC HEALTH EFFECTS

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Ashley Spooner

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Thesis written by

Ashley Spooner

Approved by

_____

Thesis Advisor

_____

Thesis Reader

Accepted by

_____

Director, University Honors Program

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PREFACE AND ACKNOWLEDGEMENTS

The following report is written in an effort to create public awareness of the harmful effects of mercury poisoning through the consumption of fish.

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INTRODUCTION

Iraq has grown its own wheat for thousands of years. In the ancient world, this portion of the Middle East, named the Fertile Crescent, was the world's breadbasket before North America took over the title. Unfortunately, the wheat crop failed in 1970. Consequently, Iraqi farmers had to place the largest commercial order in history to obtain seed grain for the following year. When the wheat was delivered in 50 kilogram sacks, the farmers noticed that the seeds were colored with a red dye, suggesting treatment with methylmercury fungicide (Clarkson & Magos, 2006, p. 631). However, the Iraqi farmers did not understand the potential toxicity of the dye and simply washed it off. They believed that they had removed the methylmercury fungicide when the red color was no longer apparent. Despite other warning signs including a written warning against eating the grain and skull-and-crossbones symbols on the bags themselves, the grain was sold and used to prepare homemade bread in Iraq (Clarkson & Magos, 2006, p. 632).

Due to the latent period of methylmercury contamination that will be discussed later, the farmers did not observe any immediate side-effects in the general population and fed the grain to their livestock. Ultimately, after about a month of exposure to the contaminated grain, Iraqi citizens first experienced paresthesia, which is the experience of tingling and numbness of a person's skin. Soon after these initial symptoms, they experienced ataxia (unsteadiness), dysarthria (a speech disorder), loss of vision, and other irreversible neurological effects. Once the problem was discovered and resolved, some individuals did have moderate recoveries, but most citizens were changed for the rest of their lives, and multiple herds of livestock were lost. This occurrence in Iraq can be

correlated with other mercury contamination problems that have adversely affected other populations. The Iraqi problem shows the effects of short term exposure. The next question becomes: what could happen to a population exposed to chronic or lifetime exposure to mercury (Clarkson & Magos, 2006, p. 632)? The following cases examine the results of this type of exposure.

The day was December 4, 1969 in Alamogordo, New Mexico and eight year old Ernestine Huckleby came home from school complaining of dizziness and pain. Ernestine's parents thought that these symptoms were from her fall off of the monkey bars earlier that day, but they knew it was more than that as she began to stagger when she walked throughout the following week. These problems continued to get worse and Ernestine was hospitalized. Initially, doctors thought that she either had spinal meningitis or a blood clot on the brain, but Ernestine's staggering continued, her vision became worse, and she began to have neurological problems (D'Itri & D'Itri, 1977, p. 41). The doctors were unable to diagnose Ernestine and subsequently released her from the hospital to be observed on an outpatient status. Ultimately, she was readmitted to the hospital and fell into a coma that lasted one year. It was later learned that methylmercury poisoning was the culprit.

As with the Iraqi grain, mercury's latent period fooled the doctors and the family, as everyone concluded that Ernestine's condition was unique to her. However, when two other family members became sick a few weeks after Ernestine, local health officials were concerned that an epidemic of viral encephalitis, which infects the gray matter of the brain, was spreading. These officials started an investigation at the Huckleby's home

that revealed the family's recent large consumption of pork from a boar that was slaughtered in September. Mr. Huckleby later commented that 14 of his feeder hogs became sick after the boar was killed and the boar itself was killed because it was showing signs of illness (Curley *et al.*, 1971, p. 65). This comment suggested to the investigators that all of the animals were also sick, possibly from eating mercury contaminated grains.

The health officials connected Mr. Huckleby's information regarding his feeder hogs and the boar to suspect methylmercury poisoning. Then, a ton and a half of grain was discovered in a locked shed on the Huckleby's farm. This grain, like the Iraqi grain, was dyed to indicate its treatment with fungicide. Ultimately, mercury poisoning was determined to be the cause of illness for the family and the hogs where, "Hair samples ranged from 186 ppm (parts per million) for Mr. Huckleby to 2436 ppm for [his daughter] Dorothy Jean, the highest level ever recorded for a human being" (Blumenthal, 1971). Once the cause was known, the sick family members were treated, but Ernestine remained blind and paralyzed, and her brother, Amos, responded poorly to the experimental drugs administered. They were transferred to the chronic care facility of the Alamogordo hospital where their recovery was very limited (D'Itri & D'Itri, 1977, p. 43).

As if the Huckleby family did not have enough problems, Mrs. Huckleby was pregnant at the time of the contamination. Her son, Michael, was born blind and retarded due to his mother's consumption of the mercury contaminated pork that resulted from the pigs eating methylmercury contaminated grains. Once Michael reached one year, his tremors were so bad that he, "…cried all day and refused to be separated from his

mother" (Snyder, 1971, p. 1014). Michael became one of the many examples and studies that show the risk from mercury contamination to fetuses and children. Not only does a mother's consumption of a product that is contaminated with mercury harm the fetus, but there are specific vaccine preservatives that are injected into children that could potentially cause adverse health effects.

Thimerosal is a vaccine preservative that contains 49.6 percent of the compound ethylmercury, a known neurotoxin. It is still used today in infant vaccines, despite the knowledge of its toxic effects. One of the many cases of thimerosal poisoning occurred in 1999 when Lyn Redwood noticed that Will, her once happy, healthy toddler, began to degenerate developmentally at 15 months (Fuentes, 2004, p. 40). He lost his speaking ability, failed to look at anyone, and appeared to be quite miserable. After Lyn completed some research on her son's symptoms and history, she came to the conclusion that Will's health problems were due to thimerosal (as cited in Fuentes, 2004, p. 40).

Many parents have faced the same tragedy as Lyn Redwood and have seen their once normal children suddenly become ill with symptoms called autism spectrum disorders (Fuentes, 2004, p. 40). These disorders include Attention Deficit Disorder, Attention Deficit Hyperactivity Disorder, Asperger's Syndrome, and, the most severe, autism. Autism in children has increased 220 percent from 10,000 children before 1980 to 22,000 American children in 2002 (as cited in Fuentes, 2004, p. 40). Although some individuals argue that this increase can be attributed to genetics and the greater awareness of autism, Lyn, science researchers, and other advocates agree that one of the key components leading to autism disorders is thimerosal (as cited in Fuentes, 2004, p. 40).

In fact, data shows that the increase in vaccines containing thimerosal correlates to the increase in autism cases. Further, the FDA and CDC did not test the safety of thimerosal until February 2000 when scientist Thomas Verstraeten provided the first of a series of studies on vaccinated children who developed neurological disorders. Most recently, Verstraeten has discovered that the risk of autism is 2.48 times greater for infants who received large amounts of mercury from vaccines. Then, in June 2000, Verstraeten also connected thimerosal with the delays in language, speech, and development for infants (as cited in Fuentes, 2004, p. 41).

The debate regarding thimerosal has gone back and forth for many years. It turns out that Verstraeten, the scientist that initially proclaimed thimerosal's effects, published a study in November 2003 that rejected his earlier findings. In this paper he states that, "All of the positive findings of neurological delays and autism have disappeared" (as cited in Fuentes, 2004, p. 42). However, it was later discovered that Verstraeten was currently employed by one of the drug companies that put thimerosal in their vaccines. It is believed that this conflict of interest led Verstraeten to dishonestly revoke his earlier findings in order to support his employer. Despite the petitions and Verstraeten's "new findings" that were used in an attempt to remove the offical toxic classification of thimerosal in an effort to support the vaccine company, it is still considered toxic. In response to Verstraeten's dishonesty in revoking his previous claims regarding the vaccine, and previous evidence of the harmful neurological effects of thimerosal, researcher Mark Geier states, "This is another powerful piece of evidence showing that thimerosal has no place in vaccines" (as cited in Fuentes, 2004, p. 42). Ultimately,

mercury containing thimerosal is still used in vaccines today, and infants, children, and adults are all at risk of high level mercury contamination. This regular use of thimerosal suggests that, "…everyone may want to read vaccine labels before being stuck with a needle" (Fuentes, 42). But beyond these very real risks in vaccines, the most significant source of mercury contamination in humans comes from fish.

In 1953, strange activity was observed among the cats that populated the Minamata Bay area. These cats exhibited neurological problems as they continuously screamed and "danced" throughout the fishing village only to end their own lives by throwing themselves into the ocean (D'Itri & D'Itri, 1977, p. 15). By 1960, the behavior seen in the cats had spread to birds, fish, pigs, and dogs. Crows regularly fell out of the sky to their deaths. The situation soon became much worse as humans were incapacitated with this mysterious disease, often many individuals in a single family (D'Itri & D'Itri, 1977, p. 15). This problem only became worse over the next 3 years because affected fisherman and their families were embarrassed by their unknown disease and failed to immediately inform anyone.

Doctors in Minamata City were alerted to the mysterious disease in 1956 when a woman brought her daughter in complaining of neurological disorders. Other cases soon followed and, similar to the Huckleby family, the doctors could not pinpoint the cause of their afflictions. As time went on, more and more Minamata fisherman were affected by what the doctors called "Minamata Disease". Once the disease had affected epidemic numbers, a committee was formed. On August 24, 1956, the medical school of Kumamoto University was directed to treat the affected patients while also conducting a

field study that would provide more information on the cause of the disease (D'Itri & D'Itri, 1977, p. 16). Between December 1953 and October 1960, the health department recorded 68 adults, 30 children, and 23 fetal victims. Out of these victims, 48 individuals died. Of this number, one-half were adults, one-third were children, and 1 out of 8 were congenital cases (Kurland, Faro, & Siedler, 1960, p. 370). The mysterious Minimata Disease had produced 850 victims by 1973. However, this figure is expected to be magnitudes higher as more studies are done to identify the number of cases of Minimata Disease during this time period.

The Kumamoto medical team attempted to collect all of the pieces to the puzzle as they interviewed the individuals who lived in Minamata Bay. Throughout this questioning process, they were comparing those families that were affected with a control group of families that were not affected. They also suspected that maybe the "mad cats" had some sort of virus that was spread to the citizens. As with any investigation, all possibilities, including the lack of sanitation and contaminated drinking water in this community, had to be examined. However, when these factors were compared with the control group, each individual had virtually the same living conditions. Therefore, the medical team quickly ruled out the possibility that Minamata Disease resulted from poor living conditions.

After questioning many citizens about their diet and drinking habits, the investigators were informed that these poor fisherman families consumed many servings of fish. In fact, "The poorest families ate the most fish, and 25 out of the 40 afflicted families ate fish from Minamata Bay every day, whereas only four other families ate as

much" (Nomura, 1968). This conclusion led to the examination of the fish in Minamata Bay. Studies indicated that the fish exhibited symptoms similar to the affected humans, and many were dying. Further, the ratio of affected adults to children that reveals more adults than children were poisoned with methylmercury could be explained because, "…some children were thought to have escaped the disease, because they left for school before the fishermen returned home and consequently ate less of the contaminated fish" (McAlpine & Araki, 1958, p. 629). Ultimately, fishing was banned in 1957 to provide another control on the study.

During the fishing ban, the number of cases reduced significantly. However, in 1958, three new patients had the disease symptoms and 16 others followed the year after. Researchers became skeptical as to whether the fish were the cause of the disease since these new patients surfaced while fishing was banned. This attitude soon changed as, "…the Kumamoto research team later concluded that the fishermen had continued to catch and eat fish and shellfish secretly, because even their very low standard of living could not be maintained without this major diet staple" (D'Itri & D'Itri, 1977, p. 18).

Once the researchers deduced that Minamata Disease was attributed to the consumption of fish, they began to investigate various sources of contamination in the water. Following extensive investigations of the water quality and factory pollutant emissions, researchers concluded that the disease was caused by some sort of heavy metal poisoning. It was not until February 1969 that crystals of a sulfur-containing methylmercuric compound were isolated from shellfish that inhabited Minamata Bay. These crystals were then synthesized in the lab and fed to cats. The cats exhibited the

same symptoms as the mad cats from 1953. When the effects on the cats were coupled with the measured mercury levels in the fish and shellfish, it was concluded that the disease was due to the mercury contamination in the fish which ultimately contaminated Minimata Bay residents (Nomura, 1968). Unfortunately, despite many extensive studies, the source of mercury that contaminated the fish and killed many people is still unknown.

The United States has begun to address the seriousness of mercury contamination in nature and in humans in order to prevent more cases, like those discussed previously, from recurring. On March 15, 2005, the Bush administration passed the Clean Air Mercury Rule in order to permanently cap and reduce mercury emissions from power plants. Although this new Environmental Protection Agency (EPA) rule is intended to reduce mercury emissions by 21 percent in 2010 from the 1999 levels of 181 tons, large factories--including coal-fired power plants and gold and sliver mines--are permitted to buy allowances for additional pollution rather than clean up their harmful production of mercury waste. Ultimately, the states participate in a cap-and-trade system in an effort to control the large amounts of toxic pollutant emissions that come from many sources. These controls operate at lower costs than if each pollutant was regulated individually. This approach first sets an overall cap that defines the maximum amount of emissions per period that will yield the desired environmental effects. Then allowances are approved by the EPA and allocated to the sources of pollutant emissions for a price as long as the number of allowances does not exceed the mandated cap (EPA, 2006). According to Felice Stadler, a mercury policy specialist, this ability of large companies and the government to negotiate mercury emissions based on the purchasing of allowances

"…gives big energy companies an extra 10 years before being required to reduce their mercury air pollution" (Barringer, 2005).

Despite the potential reduction in emitted mercury that the Clean Air Mercury Rule may attain, the ability of companies to purchase emissions allowances will lead to highly concentrated mercury emissions in some areas. This increased emission will then lead to significant health problems to the surrounding populations (Barringer, 2005). Felice Stadler represents many of the environmental groups and other people that express great concern regarding the selling of pollution allowances. As an advocate for reducing mercury emissions, she refers to the Clean Air Mercury Rules as, "…an ill-conceived plan that puts the future of our children and natural places at risk" (Barringer, 2005). Stadler and other individuals recognize that the past few decades have revealed that human contact with mercury causes deleterious health effects. Therefore, advocates against the Clean Air Mercury Rule believe that this heavy metal is too hazardous to be included in a market-based regulation that ultimately provides uneven enforcement and leaves some populations more exposed to harm than others (Barringer, 2005). Many events support these concerns associated with the Clean Air Mercury Rule. Incidents of mass poisoning reveal the most about the extremely toxic effects of mercury.

Although a consideration of the larger public policy issues concerning regulation of mercury emissions is beyond the scope of this paper, it will examine the process of mercury bioaccumulation in fish, and the subsequent contamination in humans, as well as the resulting health effects. Then, the conclusions of these processes will be applied to

shed light on the source of mercury contamination in cases like the deathly epidemic in Minamata Bay, and to address the challenge of protecting human health.

THE CHEMISTRY AND DETECTION OF MERCURY

Although scientists deduced that the mysterious disease that infected many Minimata Bay citizens was due to fish, they initially did not believe that methylmercury was the culprit. Rather, before any significant studies were conducted, they concluded that methylmercury was merely a byproduct from the industrial processes of making plastics and alkylmercury fungicides. Before 1960, the accumulation of mercury deposits in water was of little concern. At that point in time, many scientists believed that the mercury was either stable on its own, or that it reacted with other elements in the water to form harmless compounds. However, Swedish scientists soon discovered that fish were being infected with methylmercury downstream from pulp and paper mills that released phenylmercuric acetate. Therefore, the natural conversion of one form of mercury to another, that is discussed shortly, refuted the belief that mercury is stable in water and indicated that mercury could be potentially harmful.

Following the initial discovery of methylmercury contaminated fish, Swedish scientists began to thoroughly observe fish that lived both upstream and downstream from the mills in the area. It was discovered that pike fish that lived downstream from the mill on a river blocked by a dam contained 5 to 10 times more methylmercury in their tissues than those that lived upstream (Johnels & Westermark, 1969). During an observation period between 1964 and 1966, fish upstream contained 0.16 to 0.83 ppm methylmercury in their tissues, which is significantly less than the fish downstream that contained 1.5 to 3.1 ppm mercury. These concentrations were significantly above the 0.5 to 1.0 ppm range established for safe human consumption which suggested that

something at the mill needed to be changed (Johnels & Westermark, 1969). Although the mill quit emitting mercury into the water in June 1965, the pike that lived downstream continued to become more contaminated with methylmercury concentrations from 3.4 to 9.8 ppm (Johnels & Westermark, 1969). This escalation was attributed to fiber deposits remaining in the river which continued to release mercury, and thus continued to contaminate the fish.

The Swedish studies of the collection of methylmercury in fish tissues, and the escalating contamination despite the halt of mercury emissions, are a prelude to two important processes that explain the reactions of mercury in water and its uptake by fish. Although the principle emissions of mercury originate from point sources predominately located in industrial regions, the global cycle of mercury leads to mercury distribution all over the world. This cycle ultimately results in elevated concentrations of mercury in Earth's oceans and on Earth's landmasses. However, the basic physical properties of mercury should be known before discussing the global mercury cycle.

Elemental mercury, Hg^0, can be both a liquid and a gas at room temperature. It does not readily dissolve in water due to its neutral charge; therefore, it is predominately found in the air. Hg^0 is also highly volatile, which means that it readily transitions to the gaseous phase, thus also contributing to its accumulation in the air. The cation, Hg^{2+} (mercuric mercury), contains two charges and is much more soluble in water. This state of mercury is not volatile. Therefore, Hg^{2+} prefers to remain in the water or in water droplets in the air where it can exist in the liquid state, and where it is more soluble.

These physical properties of mercury create the cycle shown in Figure 1 that illustrates the movement of mercury from the water to the atmosphere (Figure 1).

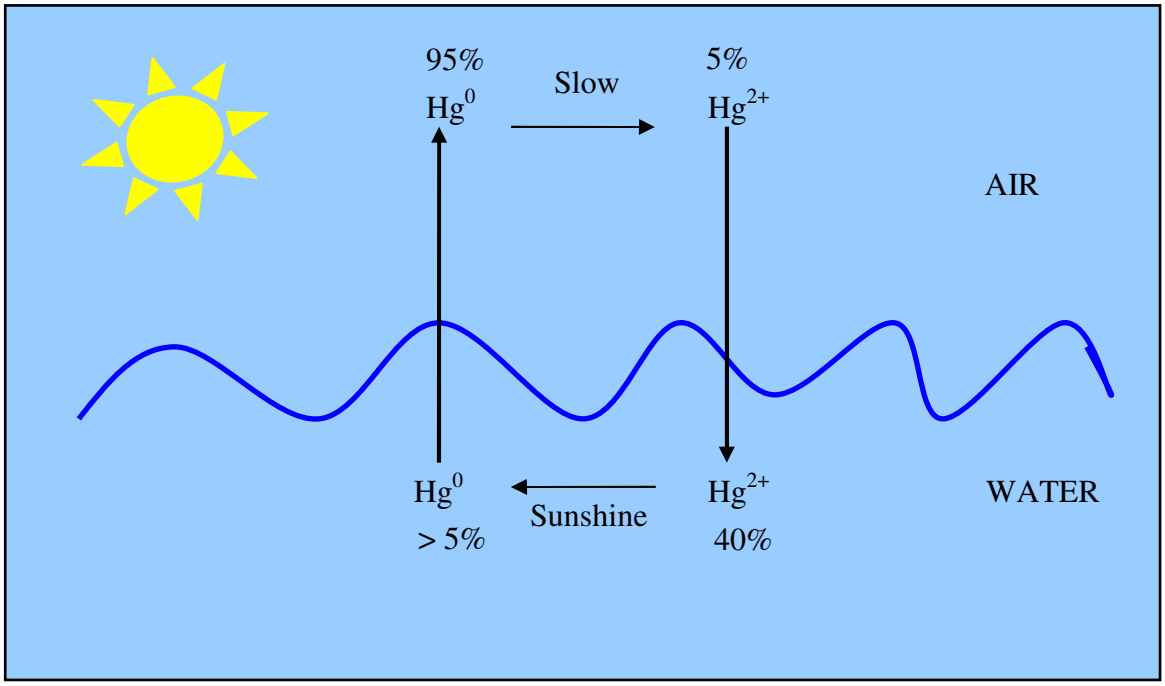

Figure 1. The Global Mercury Cycle. (adapted from Morel, Kraepiel, & Amyot, 1998, p. 545)

In Figure 1, the process of oxidation in the air, where Hg^0 loses two electrons to form Hg^{2+}, is slow because Hg^0 is highly volatile and insoluble in water. However, once Hg^{2+} is formed, it then deposits into the water where it ultimately undergoes reduction, the gaining of electrons, to form Hg^0 which then volatizes into the air. This reduction process is at its highest rate on summer days because the photoreduction of Hg^{2+} in shallow waters is at its peak. This photoreduction utilizes sunlight to convert solar energy into chemical energy and causes Hg^{2+} to gain two electrons and form Hg^0. The

cycle continues as Hg^0 volatizes back into the atmosphere where it will eventually be oxidized back into Hg^{2+} (Munthe, 1992).

Due to the relatively slow rate of oxidation of Hg^0 to Hg^{2+} is capable of remaining in the atmosphere for up to one year. This allows the mercury, in the form of Hg^{2+}, to spread over the entire planet before being deposited into the land and sea. Figure 1 shows that atmospheric mercury deposits 60% Hg^{2+} to land and the remaining 40% to water (Mason, Fitzgerald, & Morel, 1994). Once Hg^{2+} is in water, it begins its transformation to Hg^0. A series of chemical, photochemical, and biological transformations convert most of the Hg^{2+} to Hg^0, which then vaporizes back into the atmosphere while leaving some Hg^0 in the aquatic sediment (Figure 1) (Mason *et al.*, 2005). By similar process, the Hg^{2+} deposited on land is reduced to Hg^0 and returns to the atmosphere. However, more mercury, both Hg^0 and Hg^{2+}, remains on land than in water due to its absorption in soils and vegetation.

The process of changing Hg^0 to Hg^{2+} and Hg^{2+} to Hg^0 continuously feeds the precipitation/volatilization global cycle, which ultimately leads to elevated levels of Hg^{2+} in water. High levels of mercury in the cycle are predominately due to anthropogenic sources that continue to emit mercury into the water and air. However, Mercury also exists naturally in the Earth's crust. Therefore, nature contributes to the global cycle of mercury through the disturbance of mercury-containing dust particles, volcanic eruptions, forest fires, and degassing from water surfaces. Despite mercury emissions from these natural sources, studies indicate that the anthropogenic sources of mercury, including the metal production, chlor-alkali, and pulp industries, waste treatment and disposal facilities,

and coal, peat, and wood burning, contribute to two-thirds of the mercury in the atmosphere today (Lindqvist *et al.*, 1991). According to a study conducted by Pai *et al.*(2000), "Anthropogenic emissions of Hg were recently estimated at 176 tons/yr for the 48 contiguous states. Of that total, 43 tons/yr were attributed to power plants, with another 14 tons/yr to municipal waste combustion, and 23 tons/yr to smelting processes" (Pai, Niemi, & Powers, 2000). The continued emission of mercury into the environment contributes to larger concentrations of Hg^{2+} being deposited through the global cycle, thus triggering the microbial uptake of mercury in water. This uptake converts Hg^{2+} to methylmercury, the form of mercury that collects in the muscle tissue of fish. Ultimately, this conversion leads to the bioaccumulation of mercury in fish which then reaches human consumers.

Although fish absorb other forms of mercury, methylmercury is more readily digested and remains in their bodies for a longer period of time. The microbial uptake of mercury is the key step in its methylation and subsequent bioaccumulation (Morel, Kraepiel, & Amyot, 1998, p. 559). Bacteria convert the available aqueous Hg^{2+} that results from the global cycle to natural methylmercury, a mercury component that also contains carbon and hydrogen. Some bacteria absorb aqueous mercury onto their cell surfaces and convert it directly to mercury vapor while others, including *Escherichia coli*, absorb the mercury into their systems where it mixes into the cytoplasm and reacts to form a different mercury compound, such as methylmercury or Hg^0 (Harris, Eisenstark, & Dragsdorf, 1954, p. 745). Near the ocean floor, microbes remove mercury from food particles and other matter by converting it to methylmercury and dispersing it into the

sediments and surrounding water. These microbes are the key producers of the methylmercury that bioaccumulates in fish.

At the cellular level, most metals enter the cell using special transport proteins that carry them through the cell membrane. One such protein, MerT transport protein, is present in bacteria that are able to transport high concentrations of mercury. This process differs at low concentrations of Hg^{2+} where the uptake of mercury into the cell occurs when mercury binds to fat molecules, which then transport the mercury through the cell membrane. Microbes in aneaerobic waters use this transport process to collect mercury. Then, once high concentrations of mercury are reached in the microbes, they facilitate a reaction that yields methylmercury.

Although the exact mechanism for the formation of methylmercury is still uncertain, scientists have concluded that this reaction takes place in anerobic waters where the sulfide compound is present. Sulfate reducing bacteria are the major sources of methylmercury in anerobic waters. Scientists have observed that this type of methylation increases to concentrations of sulfate up to 200-500 μM (micro-molar) (Gilmour & Henry, 1991). This characteristic indicates that methylation using sulfate reducing bacteria does not occur in most estuaries and seawater. However, photochemical processes that utilize humic acid or acetate in natural waters can also form methylmercury in these places. Methylmercury is then able to enter the aquatic food chain after it is produced through the microbial uptake process discussed previously.

High concentrations of mercury in fish are reached through the biomagnification of mercury in the food chain. According to the principle of biomagnification, the

concentration of mercury will increase at higher levels in the food chain because organisms at each level of the food chain take up contaminants more rapidly than their bodies can eliminate them (Morel, Kraepiel, & Amyot, 1998, p. 560). Therefore, if it exists in high concentrations, mercury must not only be taken up by the microorganisms at the bottom of the food chain, but also must remain in the fish and passed on to their predators. Methylmercury is important in biomagnification because it is a reactive substance that is absorbed and retained in cells, which results in the methylmercury collecting in muscle tissue. Hg^0 is not bioaccumulated because it is not reactive and cannot be retained by the microorganisms. Ultimately, methylmercury is the chief component of bioaccumulation in fish, even when the concentration of Hg^{2+} exceeds that of the concentration of methylmercury.

Once mercury has bioaccumulated in microorganisms, it continues to biomagnify further up the food chain (Figure 2). Methylmercury moves higher up the food chain to humans and other predators through the ingestion of methylmercury-containing animals like fish. Therefore, the top predators on the food chain will have a higher methylmercury concentration than those below. For example, carnivorous species of fish that exist at the top of their food chain can have mercury tissue concentrations that are 10,000-100,000 times the concentration of mercury that exists in the waters that surround them (Callahan *et al.*, 1979; WHO, 1991). Consequently, these high mercury concentrations are transferred to humans that consume the fish, thus contributing to high levels of mercury concentration and the subsequent toxic health effects (Figure 2).

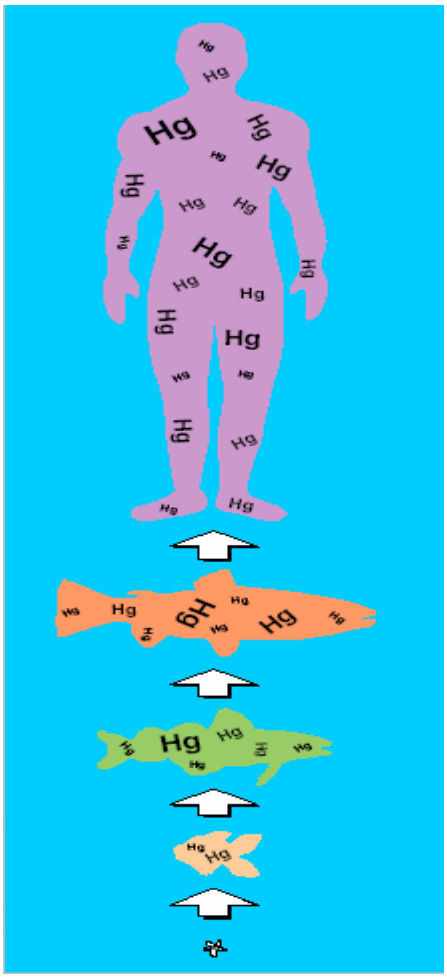

Figure 2. Biomagnification of Mercury. Mercury biomagnifies from the bottom to the top of the food chain. Even at very low exposures to aquatic ecosystems that are remote from point sources, the effects of biomagnification can result in methylmercury levels of toxiclogical concern (taken from USGS, 1995).

The primary source of mercury in humans is methylmercury contaminated fish. Unfortunately, the methylmercury in fish muscle is bound to protein which prevents the contamination from being removed by any type of skinning, trimming, or cooking (EPA, 2001). This inability to remove mercury means that approximately 95% of the methylmercury in fish is absorbed into the human body (Clarkson, 1997). Following ingestion, the mercury travels quickly throughout the body through the absorption of methylmercury by the stomach into the bloodstream which makes it possible for an amino acid carrier to transport mercury across the blood-brain barrier. This transport could result in the accumulation of the toxic metal in the brains of both fetuses and

adults. In pregnant women, methylmercury will traverse across the placenta and collect in the blood, brain, and tissues of the fetus. Both the widespread, quick diffusion of mercury into the body, and its potential harmful effects require an effective way to determine the mercury concentrations in the body, namely bioindicators.

Many bioindicators for measuring mercury exist, including: hair, blood, cord blood, and breast milk. Blood and hair are the most common bioindicators used to determine the concentration of methylmercury in the adult human body while cord blood is used to determine concentrations in fetuses. Blood levels of mercury can be detected indirectly by urinalysis. With this assay, the most recent exposure to methylmercury can be determined to aid in the determination of the time of and amount of methylmercury exposure (National Research Council, 2000). Since the source of methylmercury is fish, the total blood concentration of mercury is closely related to the amount of mercury-contaminated fish consumed.

It is estimated that hair grows 1.1 cm per month (National Research Council, 2000). This knowledge is used to cut segments of hair that correlate with historical events in the human's life, including pregnancy, breast feeding, and birth. The mercury concentrations at each segment are analyzed in conjunction with the estimated blood concentration at those times to indicate whether the person should be concerned about exceeding the Environmental Protection Agency's reference doses.

While urinalysis detects the most recent exposure to methylmercury, hair tests for mercury indicate long-term exposure that is based on the length of the hair analyzed. The protein in hair, keratin, requires amino acids as substrates to synthesize and grow.

Therefore, the keratin attracts the amino acid carrier containing the methylmercury and the mercury accumulates in the hair (Clarkson & Magos, 2006, p. 629). This mechanism indicates that the methylmercury-amino acid complex concentration is directly proportional to the plasma concentration, which is the first step in the path of mercury transport to the brain. This correlation allows the hair test to be used in conjunction with the urine test to determine blood concentration history, which is useful in the determination of methylmercury exposure history when someone is exhibiting symptoms of contamination (Clarkson, 1997).

Extensive studies on the bioaccumulation of methylmercury in the human body and the half lives of different forms of mercury have resulted in the reference doses, RfD, established by the Environmental Protection Agency, EPA. The average half-life, the time required for the quantity of substance to decay to half of its initial value, of methylmercury in blood is 70 days in adults, 90 days in children, and 46 days in lactating women (Mahaffey & Rice, 1998). In 2001, the EPA published the current RfD of methylmercury intake as 0.1 μg/kg of body weight per day (National Research Council, 2000). This RfD is considered a safe intake for all fish consumers, but it is still recommended that pregnant or breast feeding women and small children abstain from any fish that are known to have high mercury levels. As Figure 2 shows, high mercury fish include those fish that exist at the top of the food chain like shark, swordfish, king mackerel, and tilefish.

Recently, in 2004, the EPA and FDA joined together to inform the general public about mercury levels in fish. These published advisories recommend consuming fish

with low mercury content including shrimp, salmon, pollock, and catfish. Also, as mentioned before, the advisories suggest that pregnant women and small children refrain from eating large quantities of fish since the toxic effects are multiplied as the mercury crosses the placenta or enters a small child's body (HHS & EPA, 2004). While the EPA and FDA published a national advisory, it is still important to pay attention to local advisories because specific cases in nearby lakes or bays cannot be applied nationwide. Many state-issued fish advisories apply to private fisherman who catch their own fish rather than buy commercial fish. Table 1 illustrates both the Omega-3 fatty acid and mercury content of various fish.

Fish/Shellfish	DHA + EPA*	Mercury†
	g/6 oz	
Salmon (Atlantic and farmed)	3.65	ND
Herring	3.42	6.8
Salmon (Atlantic and wild)	3.13	ND
Whitefish	2.74	11.9
Anchovy	2.46	6.8
Oyster (Pacific)	2.34	ND
Mackerel (Atlantic)	2.05	8.5
Sardines (Atlantic and canned)	1.67	3.4
Trout	1.59	5.1
Bass (saltwater)	1.30	45.9
Pollock	0.92	10.2
Whiting	0.88	ND
Flatfish	0.85	8.5
Crab (blue)	0.81	10.2
Oyster (eastern and farmed)	0.75	ND
Crab (Alaskan king)	0.70	10.2
Snapper	0.55	32.3
Shrimp	0.54	ND
Tuna (light and canned)	0.46	20.4
Catfish	0.40	8.5
Haddock	0.40	5.1

ND = No data; mercury concentration below the level of detection (0.001 μg/g).
*From US Department of Health and Human Services and US Department of Agriculture. *Addendum A: EPA and DHA Content of Fish Species (Data from NDB SR 16-1).* Available at: http://www.health.gov/dietaryguidelines/dga2005/report/HTML/table_g2_adda2.htm. Accessed April 7, 2006.
†From US Food and Drug Administration. *Mercury Levels in Commercial Fish and Shellfish.* Available at: http://www.cfsan.fda.gov/%7Efrf/sea-mehg.html. Accessed April 7, 2006.

Table 1. Mercury Concentrations in Fish. Omega-3 Fatty Acid and Mercury Levels of Various Fish based on a 6 oz. serving per week (taken from Sohyun & Johnson, 2006, p. 252)

The fish advisories are intended to create awareness among fish consumers. However, this is a trade-off between the potential harm of mercury contamination that is discussed in the following chapters versus the healthful aspects of consuming fish. Fish contain many healthy vitamins like Omega-3 and provide a good source of protein. However, as shown in Table 1, it is difficult to find a fish that is high in Omega-3 fatty acids and low in methylmercury concentrations. Ultimately, if humans eat more mercury contaminated fish than the body can excrete, then the mercury concentration levels will continue to rise in the body. These elevated mercury levels will increase the likelihood of adverse health effects from the toxic metal, thus causing more cases like Minimata Bay to occur. The following chapters will examine various toxic effects that are attributed to mercury contamination in the human body.

MERCURY HEALTH EFFECTS ON ADULT HUMANS

Due to the global cycle and the bioaccumulation of mercury in the environment, human exposure to this element has become a matter of worldwide concern. Methylmercury exposure is of specific concern because the human body does not have a well developed defense mechanism against the mercury toxin (USGS, 1995). Regardless of the fact that the toxicity of methylmercury affects each individual differently, it has been proven that high concentrations of methylmercury in the human body adversely affect health. Figure 3 illustrates some of the known effects attributed to methylmercury exposure (ATSDR, 1997; EPA, 1997).

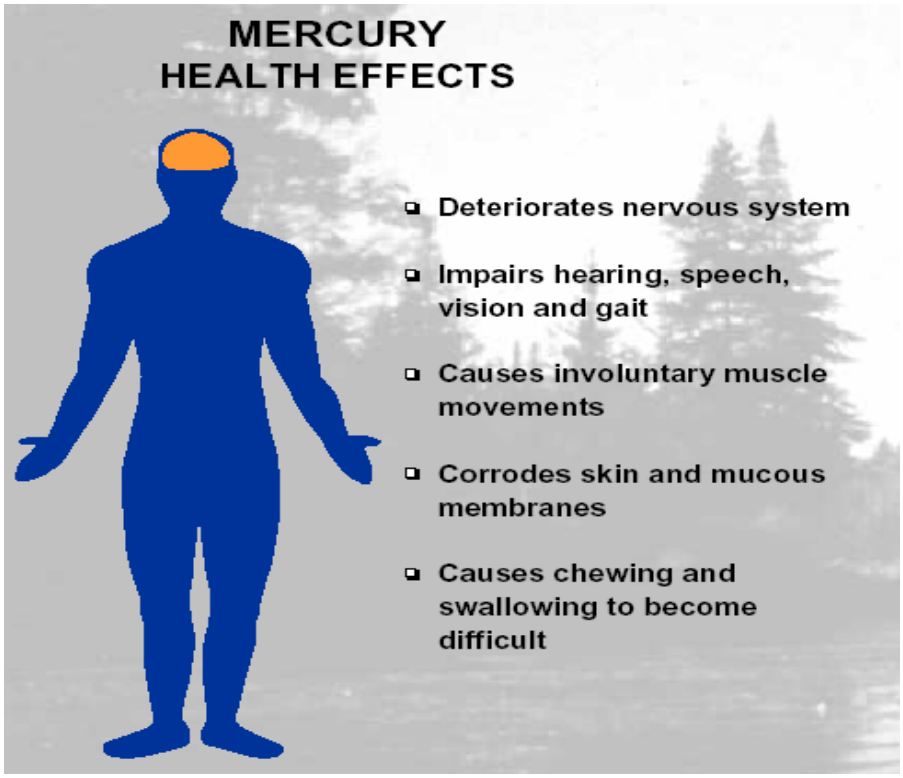

Figure 3. Mercury Health Effects (taken from USGS, 1995)

Through many studies, scientists have concluded that a single dose of methylmercury can cause the same toxic effects as those of a chronic dose. Therefore, humans that are exposed to large concentrations of methylmercury either once or over a period of time are at equal risk (Clarkson & Magos, 2006, p. 630).

The ability for methylmercury to damage the central nervous system was first discovered in London in the 1860s after the first synthesis of dimethylmercury in the laboratory (Hunter, 1969). Because dimethylmercury is a high vapor pressure liquid, it can be absorbed into the body through either inhalation or skin contact. The two chemists working in the lab to synthesize the compound exhibited early symptoms of numbness of the hands and feet that quickly deteriorated to incoordination, dysarthria, loss of vision and hearing, and other signs that indicated severe damage to the nervous system. Unfortunately, the chemists' condition continued to deteriorate and they both died shortly after their exposure to this fatal element.

The London incident provided a warning to other chemists working with compounds in the same family as methylmercury, and it was well into the 1900s before two cases similar to the London case were seen. The first case of the 1900s occurred after a chemist synthesized dimethylmercury over a three month period (Pazderova *et al.*, 1974). Soon after the chemist's exposure to the mercury, he experienced numbness and tingling in his fingertips and lips followed by a rapid deterioration that included slurred speech and the inability to recognize his relatives. Eventually, the chemist developed pneumonia and died approximately 50 days after the end of his exposure. At the time of

death, the concentration of mercury in his brain was 13.2 – 14.2 µg/g (Pazderova *et* al, 1974).

The second severe case of the 1900s occurred in a chemical laboratory at Dartmouth College in August 1997 (Nierenberg *et al.*, 1998). One of the college professors was using dimethylmercury to calibrate an instrument that was being used in a study on the toxicology of metals. After revisiting her laboratory notebook, investigators discovered that she accidentally spilled a few drops of the methylmercury onto her latex gloves. No adverse effects were felt, so the professor continued to work. However, approximately 5 months later, the professor was admitted into the hospital complaining of a gradual deterioration in balance, gait, and speech over a period of five days. The professor also indicated that she had lost 15 pounds in a period of 2 months and had several instances of nausea, diarrhea, and abdominal pain. The clinical examination supported the professor's claims of dysmetria, the inability to make limbs move with intention, a widely-based gait, and slurred speech. After being admitted to the hospital, the professor continuously deteriorated until she became completely unresponsive to all visual, verbal, and light touch stimuli on February 6, 1998, 22 days after initial symptoms and 176 days after exposure (Nierenberg *et al.*, 1998). Despite extensive medical care, the professor died months later.

The case regarding the Dartmouth College professor illustrates an extremely hazardous property of methylmercury: the latent period between exposure and the onset of symptoms (Clarkson & Magos, 2006, p. 630). As with the case of the professor, a methylmercury exposure may not initially seem hazardous, but surfaces later on, thus

allowing the toxic effects to linger within the body before treatment. This time without treatment makes it increasingly more difficult to treat the mercury poisoning and results in a greater probability that chronic or fatal effects will occur.

Following the death of the professor, a single strand of her hair was examined for mercury content. This strand confirmed that the professor had a single exposure to methylmercury at the date indicated in her laboratory notebook. Figure 4 shows the latent period of the exposure with the exponential decline in mercury concentration that shows a half-life of approximately 75 days, which is close to the accepted half-life of 70 days. Again, it was this latent period that led to late detection of methylmercury poisoning, thus resulting in delayed treatment and death.

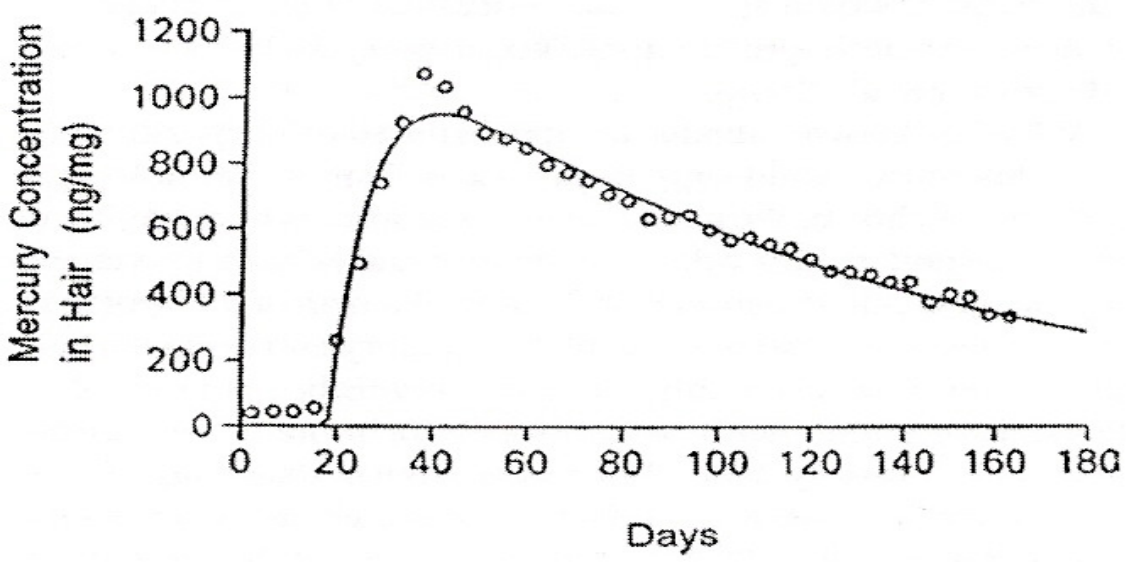

Figure 4. The concentration of mercury, ng/mg (nanogram per milligram), of a single strand of hair before and after a single exposure to dimethylmercury. The beginning of the sharp rise in mercury levels indicates the day that the exposure took place. (taken from Nierenberg et al., 1998)

The maximum hair concentration level of 1100 ppm shown in Figure 6 is consistent with published data that indicates severe poisoning at these levels. Other tests coupled the professor's hair and blood levels to deduce that she absorbed a maximum 0.44 mL of the dimethylmercury (Nirenberg *et al.*, 1998). This small amount of absorbed mercury that resulted in death shows the extreme toxicity of this metal, and the importance of monitoring mercury levels in the body since the symptoms may not be immediately detected. Although the previous cases of methylmercury poisoning did not involve ingesting the compound with regular fish consumption, a study conducted by Kawasaki et al. in 1986 concluded that a regular diet containing methylmercury has similar neurological effects as the aforementioned cases.

The Kawasaki *et al.* study added doses of 10, 30, 100, and 300 µg Hg/kg/day in the form of methylmercury chloride to the diets of four groups of macaque monkeys (Kawasaki *et al.*, 1986). The two groups that received the lower doses were studied for 52 months with the mercury dose added to the diet each day. At the conclusion of 52 months, the monkeys were sacrificed and autopsied. The group that received 100 µg Hg/kg/day was terminated between 6 and 8 months while the group receiving 300 µg Hg/kg/day was terminated after 2 months because 5 of the animals in each group either died or had to be sacrificed due to the declining condition of the animal (Kawasaki *et al.*, 1986).

Table 2 displays the concentrations of both methylmercury and inorganic mercury in different portions of the monkeys' brains. These concentrations were obtained by

taking cross-sections of the monkeys' brains and analyzing them for methylmercury content.

Dose in μg/kg/day (total exposure period)	*n*	Methyl Hg (μg Hg/g)		Inorganic Hg (μg Hg/g)	
		Occipital lobe	Cerebellum	Occipital lobe	Cerebellum
Control	5	0	0	0.014	0.014
10 (52 months)	5	0.40	0.02	0.30	0.62
30 (52 months)	5	1.01	0.07	1.33	1.95
100 (6–8 months)	4	13.2	5.08	0.13	4.87
300 (2 months)	4	24.00	9.80	0.5	8.5
100 (7 months)	1	0	0	1.5	0.8
300 (2 months)	1	0	0	0.14	0.17

Table 2. The concentrations of methylmercury and inorganic mercury in the occipital lobe and cerebellum of macaque monkeys receiving methylmercury chloride added to their diet (taken from Kawasaki et al., 1986).

As shown in Table 2, damage was observed in the neurons of the occipital lobe, not in the cerebellum, of the two higher dosage groups of monkeys. Although the methylmercury concentrations were extremely elevated in the occipital lobe, the inorganic mercury concentration lay within the same range of the two lower dosage groups where no damage was observed. The highest levels of inorganic mercury are located in the cerebellum where no damaged neurons were found upon examination. This lack of neuron damage supports previous claims from other studies that damage to neurons is associated with levels of methylmercury rather than inorganic mercury (Magos *et al.*, 1985).

Table 2 also shows the difference in mercury levels between non-human primates and adult humans. The non-human primates contain no damage to the cerebellum despite increased methylmercury levels. In adult humans, increased levels of methylmercury damage the granule cells of the cerebellum (Clarkson & Magos, 2006, p. 634). The

reason for this difference between animals is unknown, but perhaps humans have a less developed defense mechanism against methylmercury contamination.

Through the Kawasaki *et al.* study, it was discovered that a rise in the dosage level of methylmercury to a specific critical level greatly increases the amount of methylmercury deposited in the adult monkey brain. This increase is out of proportion to the increase in dose (Kawasaki *et al.*, 1986). Table 2 shows that, over a threefold range of the two lower dosage groups, the levels of methylmercury in the occipital lobe and the cerebellum increase proportionally to the increase in dose by a factor of 3. However, in the larger dosage monkeys, the concentration of methylmercury in the brain increases sharply with the next increase in dosage rate from 30 to 100 µg Hg/kg/day even though the period of exposure was much less. This jump in brain mercury levels with varied exposure rates cannot be fully explained, but it may be attributed to the fact that methylmercury binds to thiols in blood plasma, thereby allowing its rapid transport across the blood-brain barrier (Kawasaki *et al.*, 1985). Yasutake et al. (1990) suggested that as the levels of methylmercury increase in the plasma, more methylmercury will bind to the plasma, thus making the methylmercury transportable, which results in the unexplained rise in brain levels.

Regardless of whether methylmercury enters the body through contact, vapors, or diet, the previous studies indicate that it is methylmercury, not inorganic mercury that damages neuronal cells and causes adverse health effects that can result in death in humans and monkeys alike. The resulting health effects are due to damage to distinct anatomical regions of the central nervous system that control sensory and motor functions

(Clarkson & Magos, 2006, p. 635). Most often, these life-changing effects including blindness, deafness, and decreased motor skills, are irreversible due to permanent damage of neuronal cells. These common symptoms of methylmercury poisoning can be preceded by a latent period that has the potential to last weeks or even months. Therefore, this delay makes it difficult to treat methylmercury poisoning because, most often, the toxic metal has already done its irreversible damage by the time the symptoms occur. Unfortunately, this damage on adult human nervous systems is only the beginning. The adverse effects of methylmercury poisoning on human health is amplified when the immature nervous systems of the human fetus and infants are involved.

MERCURY HEALTH EFFECTS ON FETUSES AND INFANTS

The adverse health effects of high methylmercury concentrations on adult humans are known to arise from damage to neuronal cells and to result in irreversible and sometimes fatal nervous system deterioration. However, the problem is not limited to adult humans. Developing fetuses and infants are particularly vulnerable to methylmercury poisoning due to their immature nervous systems (Risher, Murray, & Prince, 2002, p. 150). The fetus can be exposed to methylmercury from the pregnant mother's placenta, and an infant is exposed through the mother's breast milk. Due to the immaturity of both a fetus' and an infant's nervous system, any exposure to methylmercury can cause irreversible nervous system damage because the contamination quickly spreads throughout the blood, brain, and other tissues (Counter & Buchanan, 2004).

The effects of high concentrations of methylmercury on the fetus and infant nervous systems were discovered after autopsies were conducted on developing human brains in both the Minimata and Iraq populations that were discussed in the Introduction. These autopsies revealed that methylmercury poisoning in developing humans can cause significantly more damage to the developing nervous system than it does with the mature adult nervous system. Unlike adult humans who only have distinct cerebellum damage due to methylmercury poisoning, an infant's entire brain is affected. Consequently, the cortical layers of neuronal cells that are observed as ordered and uniform in the normal human brain are completely distorted in a poisoned fetus or infant's brain. The autopsies

also revealed that methylmercury poisoning inhibits neuronal migration, thus causing the failure of some neurons to reach their final anatomic destination (Choi *et al.*, 1978).

It is clear that high concentrations of methylmercury in a developing human body severely damage the brain. In severe cases, like those exhibited in Minimata and Iraq, the fetus or infant will have irreversible health effects that are more likely to be fatal than in adult humans. Studies show that prenatal and postnatal exposure to methylmercury can cause permanent defects in tendon development, poor language improvement, impaired attention abilities, decreased memory, and impaired motor functions in infants and children (Castoldi *et al.*, 2001).

Less severe cases of methylmercury poisoning where the infant is apparently normal clinically, but has a history of slow development have been used to study whether methylmercury hair levels in the mother can predict defects in the infant (Marsh *et al*., 1987). Initially, a hair analysis was conducted in Iraq where the population was eating bread made with methylmercury contaminated grains. A hair sample of a mother was taken in 1973, months after her pregnancy. Scientists were able to trace back to the period of intake by measuring the hair centimeter by centimeter from the scalp down to the other end to create the graph in Figure 5. This measurement accurately traced the peak methylmercury concentration levels back to 1972 when the population was eating the contaminated grains. Finally, a blood sample was also taken to ensure accurate data and, as Figure 5 shows, the blood sample is parallel to the hair sample, thus indicating accurate results.

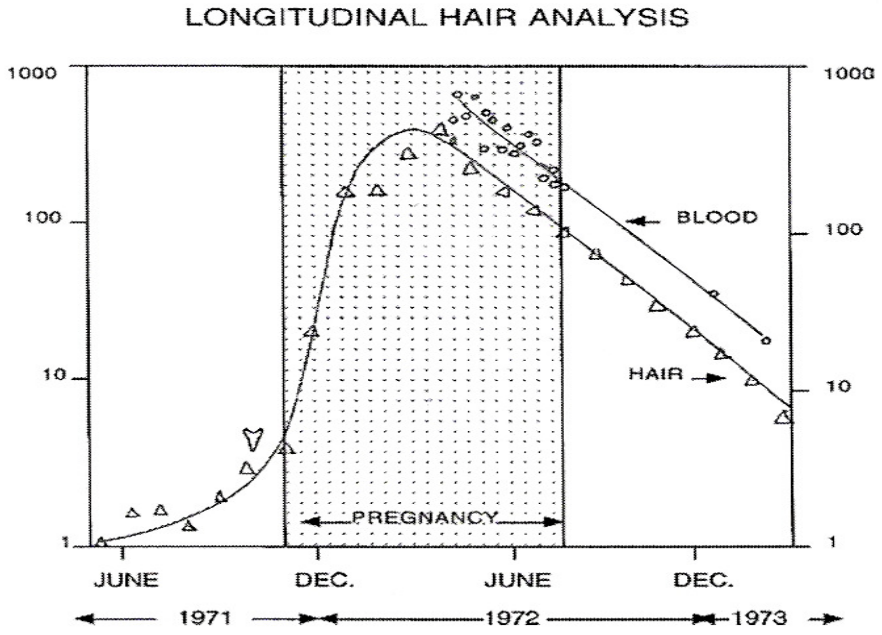

Figure 5. Hair Analysis. The concentration of mercury in consecutive 1-cm segments of a maternal sample and corresponding concentration in blood samples. The dotted band is the period of pregnancy. The vertical arrow indicates the estimated date for the start of consumption of the contaminated bread. (taken from Clarkson & Magos, 2006, p. 636)

Once the peak levels of methylmercury were found from the hair analysis, scientists interviewed the family to determine the date of birth of the observed mother's child. Further questions regarding when the child first began to walk and other significant developmental milestones were used to define a timeline of development. This timeline was used in conjunction with the mother's hair analysis to determine whether methylmercury concentrations in the pregnant mother caused damage to her fetus.

This prenatal study led to the final conclusion that there is a dose-response relationship, a change in effect on a human caused by varying levels of exposure to a substance, between the amount of methylmercury that the fetus is exposed to and the

probability for neurological problems. This relationship is based on the peak level of methylmercury concentration in the pregnant mother versus the incidence of delayed development and the presence of neurological disorders (Cox *et al.*, 1989). The dose-response relationship for a case where the onset of walking past the age of eighteen months was considered "delayed" is shown in Figure 6.

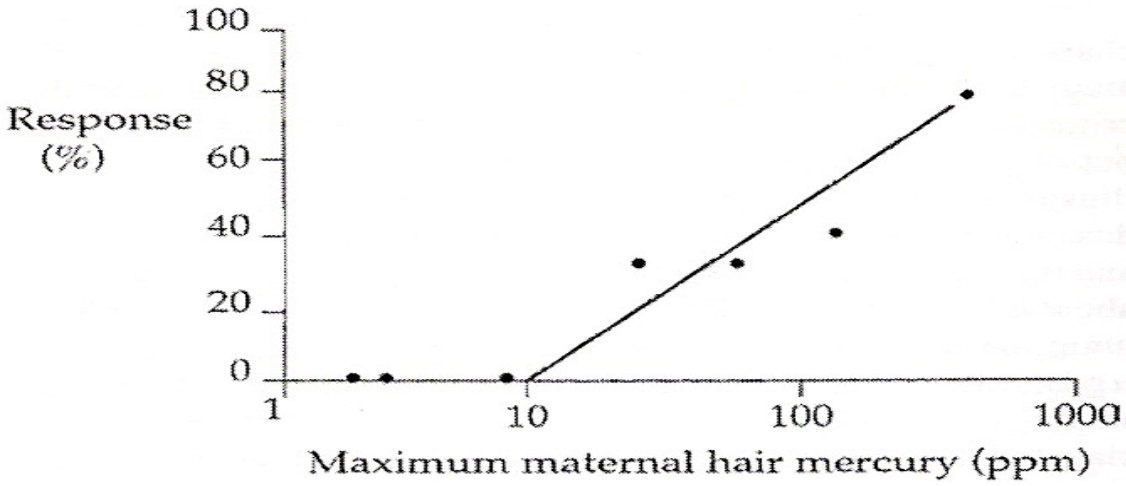

Figure 6. Prevalence of An Infant's Delayed Development In Walking versus The Concentration of Methylmercury in Maternal Hair During Pregnancy. (taken from Clarkson & Magos, 2006, p. 636)

The response indicates the prevalence of delayed development increases at higher concentrations of methylmercury in the mother. Ultimately, these results show that the fetus begins to have developmental problems with maternal hair concentrations higher than 10 ppm. This low threshold level contrasts with adult threshold level of 100 ppm before experiencing adverse health effects, thus confirming that the fetus' brain is significantly more sensitive to methylmercury.

The prenatal study in Iraq caused concern for the fish-eating populations in other parts of the world. Both the scientists and the fisherman in these areas recognized that the 10 ppm threshold suggested by the Iraq study could be easily exceeded through their normal fish diet, thus putting their unborn fetuses in harm's way. This concern led to many studies directed at determining whether fish consumption causes adverse health effects in infants.

Most recently, a small group of infants that were prenatally exposed to methylmercury in the Philippines was examined (Ramirez *et al.,* 2000). Seventy-eight infant-mother pairs were tested to determine the initial concentration of methylmercury in hair, blood, milk, and other biological media. Forty-six of the infants were then observed in a follow-up study at 2 years of age and were compared to forty-six control infants who were not exposed to methylmercury. This follow-up indicated that delayed neurodevelopment and linguistic problems in infants are attributed to prenatal methylmercury exposure (Ramirez *et al.*, 2003). Although this study in the Philippines supports the conclusions made in the Iraq study, three major studies conducted in this field have drawn more attention to the methylmercury problem: The New Zealand Study, The Faroes Study, and The Seychelles Study.

The New Zealand Study was composed of three different ethnic groups: Maori, Polynesian, and descendents of Caucasian immigrants. These populations were known to consume fish and chip type meals that contained mainly shark with on average high methylmercury content of 4 ppm. The first observation in these populations was conducted on 935 women who claimed to eat fish more than three times each week

(Kjellstrom *et al.*, 1986). A hair analysis like the one shown in Figure 8 was done on these women and the study concluded that seventy-three women had average methylmercury hair levels exceeding 6 ppm during pregnancy.

The seventy-four children in the high mercury exposure group were matched with another child with low mercury exposure based on ethnicity, location of delivery, the mother's age, and the child's age. Thirty-eight high mercury exposure and thirty-six low mercury exposure children were tested with the DDST, Denver Developmental Screening Test, at 4 years of age. Results indicated that 52% of the high mercury exposure children versus 17% of the low mercury exposure reference group had abnormal DDST results (Kjellstrom *et al.*, 1986).

Approximately 2 years later, children in the New Zealand group that had maternal mercury concentrations greater than 6 ppm were matched with three control children based on ethnicity, sex, mother's age, mother's smoking, current residence, and duration of residence in New Zealand (Kjellstrom *et al.*, 1989). Two of the control children had maternal methylmercury hair levels below 3 ppm while one control child had hair levels between 3 and 6 ppm. Ultimately, 237 children were examined where the hair levels in the high mercury exposure group averaged 8.3 ppm with a range of 6 to 21 ppm. Each child underwent twenty-six various tests that covered general knowledge, language development, motor skills, ability to attain information, and social skills. Test results indicated that poor scores were prevalent in the high mercury exposure group for children with maternal hair levels of 13 to 15 ppm with a peak monthly average of 25 ppm during

pregnancy (Kjellstrom *et al.*, 1989). A comparison of these results with other studies will be made below.

The Faroes population, located in Northern Europe between the Norwegian Sea and the North Atlantic Ocean, regularly consumes whale meat that contains an average of 1.6 ppm methylmercury (Grandjean *et al.*, 1992). However, it is important to note that there is also consumption of PCBs and other organic pollutants from the whale blubber. In this study, a group of 1022 infants was assembled from hospital births in the Faroe Islands over a twenty-one month period (Grandjean *et al.*, 1992). Scientists then interviewed the infants' families to create a timeline of developmental milestones that occurred during their children's first year (Grandjean *et al.*, 1995). After collecting data for 583 children, three milestones including, sitting without support, crawling, and ability to get to the standing position, were chosen for comparison. These results indicated that reaching these three milestones could not be correlated with maternal hair methylmercury levels.

More tests were done on the same children once they reached 7 years of age. 112 children with average maternal hair methylmercury levels between 10 and 20 ppm during pregnancy were compared with another group of children with maternal hair levels that were less than 3 ppm (Grandjean *et al.*, 1998). Once testing was completed, six out of the eighteen motor and verbal capabilities were significantly lower for the high mercury exposed children. These capabilities included finger tapping, hand-eye coordination, Boston Naming Test, and the California Verbal Learning Test. The results from this study differ from the main study that was conducted when the children were infants,

suggesting that methylmercury could be the cause for developmental problems, but there is not enough substantial evidence to fully make this claim.

The Seychelles Study is similar to the New Zealand Study, however, the population's fish consumption consisted of a daily diet of a wide variety of ocean fish that contained methylmercury concentrations approximately ten times lower than those of the New Zealand and Faroes populations (Shamlaye *et al.*, 1995). 789 infants between the ages of 5 and 109 weeks, with an average prenatal methylmercury exposure of 6.1 ppm based on maternal hair levels, were observed by a neurologist. Studies including the revised Denver Developmental Screening Test (DDST-R) were conducted on the infants as well as other neurological tests. The tests reveal that there was no correlation between the maternal methylmercury hair levels and abnormal test results.

A pilot group consisting of 740 infants that were 6.5 months old with a median maternal methylmercury hair level of 5.9 ppm was established as a reference for the main group (Marsh *et al.*, 1995). The DDST-R and the Fagan Test of Infant Intelligence (FTII) were given to each infant. The results of these tests on the pilot group supported those of the main group and concluded that the maternal methylmercury hair levels of pregnant women in this population did not adversely affect the health of the infants.

More tests were conducted on both the main and pilot groups of Seychelles infants with the results shown in Table 3.

Age (months)	Cohort	Type of test	Test outcomes		
			Adverse	Beneficial	Neutral
1–22	Pilot	Neurological			3
		DDST	1		
6.5	Main	Neurological			3
		DDST			1
		Visual Recog.[a]			1
		Visual Memory[a]			1
19	Main	Milestones[b]			3
19	Main	Milestones			3
19	Main	MDI[c]			1
19	Main	PDI[c]			1
29	Main	MDI[c]			1
29	Main	PDI[c]			1
29	Main	Inf. Behavior	1(M)	5	
66	Pilot	Comprehensive[b]	1		8
66	Main	Comprehensive		1	5
109	Main	Comprehensive	1	1	19
1–109	Both	All	4	2	56

Note: (M) In males only.
[a]The Fagan Test of Infant Intelligence.
[b]After removal of outliers.
[c]The Bayley Scales of Infant Development.

Table 3. Outcomes of Neurological Tests on Seychellois Children Exposed to Average Levels of Methylmercury in the Womb. (taken from Clarkson & Magos, 2006, p. 641)

The adverse effects tabulated in Table 3 can be attributed to the mother's IQ, socioeconomic status of the family, and the home environment, but are not correlated with levels of methymercury exposure in the womb. The Seychelles Study is one of the largest groups ever examined and is the only group to be examined over a period of 9 years. However, regardless of how well this study was conducted, it cannot claim that there are no risks involved with infant exposure to methylmercury, it can only establish a limit to the degree of risk at specific maternal methylmercury hair levels.

Conclusions from these three studies suggest that there is a correlation between maternal hair levels and developmental problems. However, a definite claim stating that

methylmercury concentrations in a pregnant mother adversely affect the health of the fetus cannot be made. A comparison of these studies with the Iraq study leads to a more educated conclusion based on many variables. Each of the four studies have been analyzed to find a no-observed-adverse-effect-level (NOAEL), the level of methylmercury exposure that can be sustained without producing adverse health effects. From these levels, a benchmark dose (BMD) is defined as the dose that corresponds to no adverse health effects, usually 5 to 10% prevalence over the control group (Crump, 1984). The benchmark lower limit (BMDL) that represents a NOAEL is calculated at two standard deviations below the BMD.

Based on estimated NOAEL data predicted by the Iraq study, there is a risk of approximately 5% prevalence in delayed developmental effects for fetuses exposed to maternal hair methylmercury levels between 10 and 20 ppm. Figure 7 illustrates the estimated NOAELs for each study.

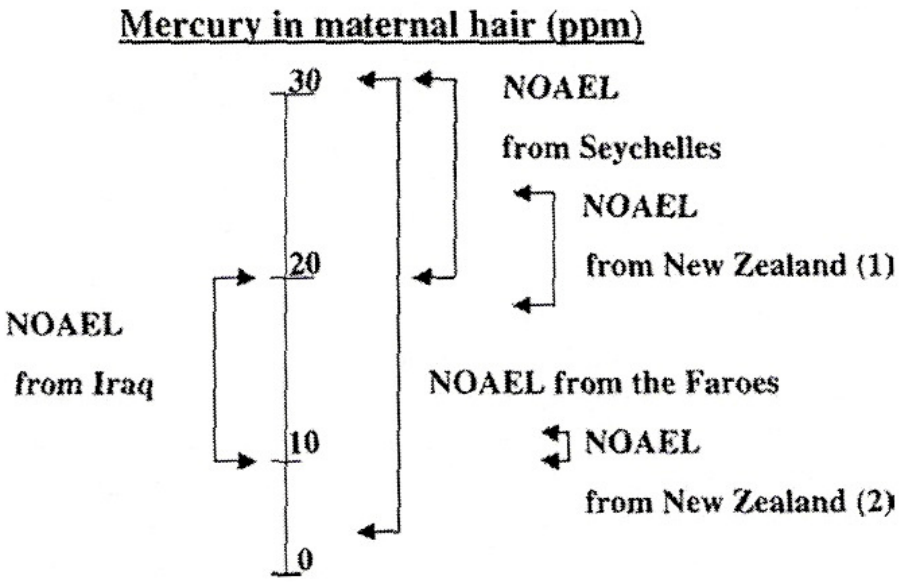

Figure 7. Comparison of NOAELs Between Iraq, New Zealand, Faroes, and Seychelles Populations (taken from Clarkson & Magos, 2006, p. 642)

Figure 7 depicts the NOAEL as mercury levels in maternal hair during pregnancy. The estimated levels for both the Seychelles and Faroes studies are at the 95% confidence limit of the benchmark dose that was set at a 10% response rate for developmental problems. Further, the first New Zealand figure is the estimate that includes all data points while the second figure omitted the highest mercury data point. The overlap in Figure 7 is considered remarkable (Clarkson & Magos, 2006, p. 642). However, the agreement shown may not be real. When the data from the three studies is compared, it is apparent that there were much fewer, if any, adverse health effects due to prenatal methylmercury exposure for the Seychelles versus the New Zealand and Faroes studies. The problem lies in determining whether these differences are due to different experimental methods, population characteristics, or the possible exposure to other toxic pollutants.

Many issues, including the differences in age observation throughout the studies, the methods used to determine the concentration of methylmercury in the body, and the possibility of exposure to other toxic pollutants in the environment, have been disputed in an effort to explain the different results from each study. Close study of these issues has led the possible contribution of the previously discussed variables to be refuted. Leaving the conclusion that, the greatest difference between these populations is the differences in diet.

The Faroes population consumes whale meat that has an average methylmercury concentration of 1.6 ppm while the New Zealand population regularly consumes shark with concentrations of methylmercury of 6 ppm. The Seychelles diet is mostly fish, but the concentration of methylmercury in the ocean fish that they consume is 10 times less than the other two populations at 0.3 ppm (Myers *et al*., 2003). These numbers indicate that the amount of methylmercury reaching the brain after each meal was 10 times more in the Faroes and New Zealand populations than the Seychelles population. Therefore, more adverse health effects in infants could have been seen in the Faroes and New Zealand populations due to the exposure to the larger concentrations of methylmercury at crucial times in development.

The comparison between the various studies that examine the effects of prenatal methylmercury exposure on infant health suggests that the risk of damaging the developing brain may depend on the manner in which the methylmercury reaches the brain. A single high mercury exposure from a meal of fish may be more harmful than a regular diet of low methylmercury-containing fish. Ultimately, it is known that the

effects of methylmercury poisoning are significantly more toxic to fetuses and infants, and scientists are still working to determine a safe low-dose benchmark. A study conducted by Knobeloch *et al.* (2005) reported that 12% of American women that were eating the EPA specified amounts of fish had hair methylmercury levels greater than the EPA guidelines. This discovery is a cause for concern for pregnant and breastfeeding women due to the known adverse effects of mercury exposure on fetuses and infants. According to Knobeloch *et al.* (2005), rather than completely eliminating fish from the diet, it is important for pregnant and nursing mothers to avoid high methylmercury containing fish. The inclusion of low methylmercury containing fish in a diet will provide the mother and the fetus or infant with the beneficial nutrients like Omega-3 fatty acids that aid in development.

PUBLIC AWARENESS OF MERCURY TOXCITY

The previous chapters have established that methylmercury is able to bioaccumulate in the environment and proceeds to bioaccumulate up the food chain, especially in fish. Humans then consume the fish and the methylmercury begins to bioaccumulate in the human body. At high concentrations, methylmercury is proven to cause irreversible and sometimes fatal neurological effects in humans, and is even more toxic to the developing nervous systems of fetuses and infants.

Despite large cases including Minimata Bay and the contaminated Iraqi grains that convey the severe toxicity of this metal, the public does not understand the importance of monitoring methylmercury concentrations in the water, fish, and the human body today. It is understood that some mercury will still be methylated in the global cycle despite a decrease in mercury emissions from manmade mills and gold mines. The biggest mercury problem lies in the contaminated waterways that have been saturated with fertilizer waste and other carbon containing wastes including wood pulp and sewage. Tests conclude that the abundant supply of mercury and carbon containing wastes from agriculture, industry, and municipal wastes have accelerated the growth of the plants that ultimately feed the microbes in the global cycle (D'Itri & D'Itri, 1977, p. 50). This acceleration is solely due to human processes that are only loosely regulated.

Although the problem of severe mercury contamination is not significant today, without change, it will become severe with time. As the population of the United States and the world continues to grow, production in mills and plants, agriculture, and municipal wastes will increase. This increase in production will consequently provide

more food to the plants that subsequently feed the microbes to accelerate bioaccumulation of mercury. If the bioaccumulation of methylmercury is accelerated too quickly, fish will have higher concentrations of mercury that will ultimately reach the humans and animals that eat the fish. Since bioaccumulation is the process of an organism taking up more contaminate than it can get rid of, humans will continue to increase the concentration of methylmercury in the body to reach the highly toxic levels that have been discussed previously (USGS, 1995). Once these toxic levels are reached, it will become more difficult to treat adults and almost impossible to treat prenatal and postnatal infants. Therefore, humans will either experience adverse irreversible neurological effects or will die.

The possibility of such a severe case of bioaccumulation of methylmercury is not unattainable. However, this problem can be easily prevented with awareness and active methods to reduce the emissions of mercury and carbon containing wastes into the water. Staged scenarios suggest that it would take eight years to see even a small reduction in methylmercury concentrations in fish if emissions were reduced by five percent (USGS, 1995). This delay in results means that action needs to be taken now, not ten years from now, which the Clean Air Mercury Rule allows when large companies buy their time through purchasing pollution allowances. It is unknown how long it would take to reach the severe case discussed above, but with continued growth and production, ten years until clean up could be too late.

Total airborne mercury emissions in the United States were reduced 5 percent from 209.6 tons to 113.2 tons from 1990 to 1999. Despite these reductions, forty-four

states have issued fish advisories calling humans to limit fish consumption in highly contaminated streams due to an increase in the mercury contamination of fish (as cited in Barringer, 2005). Unfortunately, many individuals are either unaware of the fish advisories or do not understand their significance and continue to eat highly contaminated fish that could eventually cause severe health problems. It is especially important for pregnant and breast feeding women that fish advisories are well known and that individuals understand what a fish advisory implies.

The public health advisory levels published by the EPA are significantly below the actual threshold of methylmercury contamination that will cause severe health effects. These levels are deliberately set low in order to ensure the safety of humans consuming fish and seafood on a regular basis (Lipfert *et al.*, 2005, p. 394). However, although these advisories are set low, it is important to use them as a guideline to how much methylmercury is being consumed with certain fish species. Awareness and knowledge of the fish advisories are a simple way to monitor methylmercury consumption and to prevent health problems caused by the toxic metal, but it is necessary for other precautions to be instituted by the government, health officials, and health advisory agencies.

Much of the mercury problem is still being studied, but it is also known that mercury is a highly toxic metal emitted by manmade processes that can cause severe neurological problems to humans. This knowledge alone should institute a "precautionary principle" which states: "When an activity raises threats of harm to human health or the environment, precautionary measures should be taken even whether some

cause and effect relationships are not fully established scientifically" (Blendon & Rogers, 1983). There are four components to the precautionary principle including: starting preventative action, shifting the burden of proof to the advocates of the harmful activity, exploring alternatives, and increasing the decision-making participation of the public. Unfortunately, there are unintended consequences associated with the precautionary principle.

The implementation of a precautionary principle would suggest removing mercury from the environment. Not only would it cost $12.00 per gram of mercury to remove the excess of 113 tons of mercury emitted into the environment each year, but other uses of mercury would be compromised (Sivrastava *et al.*, 2001). For example, thiomerosal, an effective children's vaccine, would be banned, and blood pressure monitors used in hospitals would be replaced with electronic devices that are less accurate. Finally, if the United States decided to sell its excess mercury stockpile in the open market, the price of mercury would decrease, thus making it more available globally to use in processes like gold mining that continue to emit the toxic pollutant into the water.

It is not an option to ask humans to remove all fish consumption from a diet due to the beneficial vitamins in fish that promote good health. However, the problem of increasing methylmercury concentrations in fish continues to become more severe. Among the many actions that need to take place, yearly physicals should include a mercury screening in order to provide early detection of potential poisoning, testing of mercury content in fish must continue, and public health advisories should be posted

wherever fish are sold (Hightower, 2003, p. 608). These simple actions will increase awareness and education for humans that participate in a lifetime of fish consumption, but continued emissions of mercury and the carbon containing wastes that feed the global cycle must be regulated.

A cost-benefit analysis that includes more than the costs discussed above needs to be conducted to determine whether it is feasible to remove mercury from the environment. Although mercury cannot be removed, it is a necessity to reduce emissions drastically by implementing regulations. If the emission of mercury and other wastes that feed the global cycle continues at the same rate or increases, it could lead to a complete ban in fish consumption or severe neurological damage to the humans that have continued to consume methylmercury contaminated fish. Ultimately, although the consumption of methylmercury containing fish is not a severe problem today, the lack of regulation and our failure to remove this toxic element from the environment will lead an increase in methylmercury concentrations in fish. These increased concentrations will subsequently be transferred to fish consuming humans causing irreversible and potentially fatal neurological effects in many humans and unborn fetuses.

BIBLIOGRAPHY

Agency for Toxic Substances Disease Registry (ATSDR) (1997). Toxicological profile for mercury. ATSDR Draft Update.

Barringer, F. (2005, March 14). Bush plan to permit trading of credits to limit mercury. The New York Times, nytimes.com. Retrieved 26 October 2006.

Blendon, R., & Rogers, D. (1983). Cutting Medical Care Costs. JAMA, 250, 1880-1885.

Blumenthal, R. (1971, June 6). In 18 months, mercury-poisoned girl almost well. The New York Times.

Budtz-Jorgensen, E., Keiding, N., & Grandjean, P. (2001). Benchmark dose calculation from epidemiological data. Biometrics, 11, 201-210.

Callahan, A., Slimak, W., Gabel, W., *et al.* (1979). Water related environmental fate of 129 priority pollutants, introduction and technical background, metals and inorganics, pesticides, and PCBs. U.S. Envrionmental Protection Agency, Office of Water Waste and Management, EPA 440/4-79-029a, 14-1 – 14-5.

Castoldi, F., Coccini, T., Ceccatelli, S., & Manzo, L. (2001). Neurotoxicity and molecular effects of methylmercury. Brain Res. Bull., 55, 197-203.

Clarkson, T., & Magos, L. (2006). The toxicology of mercury and its chemical compounds. Critical Reviews in Toxicology, 36, 609-622.

Clarkson, T. (1997). The toxicology of mercury. Crit. Rev. Clin. Lab Sci., 34, 369-403.

Choi, H., Lapham, W., Amin-Zaki, L., & Saleem, T. (1978). Abnormal neuronal migration, deranged cerebral cortical organization, and diffuse white matter astrocytosis of human fetal brain: A major effect of methyl mercury poisoning *in utero*. J. Neuropath. Exp. Neurol., 37, 719-733.

Counter, A., Buchanan, H. (2004). Mercury exposure in children. Toxicol. Appl. Pharmacol. 198, 209-230.

Cox, C., Clarkson, T., Marsh, D., Amin-Zaki, L., Tikriti, S., & Myers, G. (1989). Dose response analysis of infants prenatally exposed to methylmercury: An application of a single compartment model to single strand hair analysis. Environ. Res., 49, 318-332.

Crump, K. (1984). A new method for determining allowable daily intakes. Fundam. Appl. Toxicol., 4, 854-871.

Curley, A., Sedlak, V., Girling, E., Hawk, R., Barthel, W., Pierce, P., & Likosky, W. (1971). Organic mercury identified as the cause of poisoning in humans and hogs. Science, 172, 65.

D'Itri P., & D'Itri F. (1977). Mercury Contamination: A Human Tragedy (pp. 15-61). New York: John Wiley & Sons.

Fuentes, A. (2004). Injecting mercury: Is thimerosal the missing link to autism and developmental problems? E Magazine, May/June, 40-41.

Gilmour, C., & Henry, A. (1991). Mercury methylation in aquatic systems affected by acid deposition. Environ. Pollut., 71, 131-169.

Grandjean, P., Weihe, P., Jorgensen, P., Clarkson, T., Cernichiari, E., & Videro, T. (1992). Impact of maternal seafood diet on fetal exposure to mercury, selenium and lead. Arch. Environ. Health, 47, 185-195.

Grandjean, P., Weihe, P., & White, R. (1995). Milestones of development in children exposed to methylmercury in milk. Neurotoxicology, 16, 27-34.

Grandjean, P., Weihe, P., White, R., & Debes, F. (1998). Cognitive performance of children prenatally exposed to "safe" level of methylmercury. Environ. Res., 77, 165-172.

Gutknecht, J., & Tosteson, C. (1973). Diffusion of weak acids across lipid bilayer membranes: effects of chemical reactions in the unstirred layers. Science, 182, 1258-1261.

Harris, J., Eisenstark, A., & Dragsdorf, R. (1969). A study on the location of absorbed mercuric ions in *Escherichia coli*. J. Bacteriol., 68, 745.

Hightower, J., & Moore, D. (April 2003). Mercury levels in high-end consumers of fish. Environmental Health Perspectives, 111:4, 604-608.

Hunter, D. (1969). Diseases of occupations. London: Little, Brown.

Johnels, A., & Westermark, T. (1969). Mercury contamination of the environment in Sweden. Chemical Fallout, Springfield, Thomas.

Kawasaki, Y., Ikeda, Y., Yamamoto, T., & Ikeda, K. (1985). Long-term study of methylmercury chloride in monkeys. Food Hyg. Soc. Jpn, 27, 528-552.

Kjellstrom, T., Kennedy, P., Wallis, S., & Mantell, C. (1986). Physical and mental development of children with prenatal exposure to mercury from fish. Stage 1 Preliminary tests at age 4. Solna, National Swedish Environmental Board. Report number 3080.

Kjellstrom, T., Kennedy, P., Wallis, S., Stewart, A., Friberg, L., Lind, B., Wutherspoon, P., & Mantell, C. (1989). Physical and mental development of children with prenatal exposure to mercury from fish. Stage 2 Interviews and psychological tests at age 6. Solna, National Swedish Environmental Board. Report number 3642.

Knobeloch, L., Anderson, H., Imm, P., Peters, D., & Smith, A. (2005). Fish consumption, advisory awareness, and hair mercury levels among women of childbearing age. Environ. Res., 97, 220-227.

Kurland, L., Faro, S., Siedler, H. (1960). Minimata Disease: The outbreak of a neurological disorder in Minimata, Japan, and its relationship to the ingestion of seafood contaminated by mercuric compounds. World Neurol., 1, 370.

Lindqvist, O., *et al.* (1991). Mercury in the Swedish environment. Water Air Soil Pollut., 55, 23-30.

Lipfert, F., Morris, S., Sullivan, T., Moskowitz, P., & Renninger, S. (2005). Methylmercury, fish consumption, and the precautionary principle. Air and Waste Manage. Assoc., 55, 388-398.

Magos, L., Brown, W., Sparrow, S., Bailey, E., Snowden, T., & Skipp, R. (1985). The comparative toxicology of ethyl- and methylmercury. Arch. Toxicol., 57, 260-267.

Marsh, D., Clarkson, T., Cox, C., Myers, G., Amin-Zaki, L., & Al-Tikriti, S. (1987). Fetal methylmercury poisoning: Relationship between concentration in single strands of maternal hair and child effects. Arch. Neurol., 44, 1017-1022.

Marsh, D., Clarkson, T., Myers, D., Davidson, P., Cox, C., Cernichiari, E., Tanner, M., Lednar, W., Shamalaye, C., Choisy, O., Hoareau, C., & Berlin, M. (1995). The Seychelles study of fetal methylmercury exposure and child development. Neurotoxicology, 16, 583-596.

Mason, P., Abbott, L., Bodaly, A., Bullock, R., Jr., Evers, D., Lindberg, E., Murray, M., & Swain, B. (2005). Monitoring the response to changing mercury deposition. Environ. Sci. Technol., 1, 15A-22A.

Mason, P., Fitzgerald, F., & Morel, M. (1994) The biogeochemical cycling of elemental mercury: anthropogenic influences. Geochim. Cosmochim. Acta., 58, 3191-3198.

Mahaffey, R., & Rice, E. (1998). Mercury Study Report to Congress. Environmental Protection Agency, Issue 09.

McAlpine, D., & Araki, S. (1958). Minamata Disease – an unusual neurological disorder caused by contaminated fish. Lancet, 2, 629.

Morel, M., Kraepiel, A., & Amyot, M. (1998). The chemical cycle and bioaccumulation of mercury. Annu. Rev. Ecol. Syst., 29, 543-566.

Munthe, J. (1992) Some aqueous reactions of potential importence in the atmospheric chemistry of mercury. Atmos. Environ., 26A, 1461-1468.

Myers, G., Davidson, P., Cox, C., Shamlaye, C., Palumbo, D., Cerinchiari, E., Sloane-Reeves, J., Wilding, G., Kost, J., Haung, Li-S., & Clarkson, T. (2003). Prenatal methylmercury exposure from ocean fish consumption in the Seychelles Child Development Study. Lancet., 361, 1686-1692.

National Research Council (2000). Toxicological effects of methylmercury. Washington, D.C.: National Academy Press.

Nierenberg, W., Nordgren, E., Chang, B., Siegler, W., Blayney, B., Hochberg, F., Toribara, Y., Cerichiari, E., & Clarkson, T. (1998). Delayed cerebellar disease and death after accidental exposure to dimethylmercury. N. Eng. J. Med., 338, 1672-1686.

Nomura, S. (1968). Epidemiology of Minimata Disease. Minamata Disease. Japan: Kumamtoto University.

Pai, P., Niemi, D., & Powers, B. (2000). A North American inventory of anthropogenic mercury emissions. Fuel Process. Technol., 65-66, 101-115.

Pazderova, J., Jirásek, A., Mráz, M., & Pechan, J. (1974). Postmortem findings and clinical signs of dimethylmercury poisoning in man. Int. Arch. Arbeitsmed., 33, 323-328.

Shamlaye, C., Marsh, D., Myers, G., Cox, C., Davidson, P., Choisy, O., Cernichiari, E., Choi, A., Tanner, M., & Clarkson, T. (1995). The Seychelles child development study on neurodevelopmental outcomes in children following *in utero* exposure to methylmercury from a maternal fish diet. Neurotoxicology, 16, 597-612.

Sivrastava, R., Sedman, C., Kilgoe, J., Smith, D., & Renninger, S. (2001) Preliminary estimates of performance and cost of mercury control technology on electric utility boilers. J. Air and Waste Manag. Assoc., 51, 1460-1470.

Snyder, R. (1971). Congenital mercury poisoning. New Eng. J. Med., 284, 1014.

Sohyun, P., & Johnson, MA. (2006). Awareness of fish advisories and mercury exposure in women of childbearing age. Nutrition Reviews, 64, 250-256.

Ramirez, G., Cruz, M., Pagulayan, O., Ostrea, E., & Dalisay, C. (2000). The Tagum study I: Analysis and clinical correlates of mercury in maternal and cord blood, breast milk, meconium, and infants' hair. Pediatrics, 106, 774-781.

Ramirez, G., Pagulayan, O., Akagi, H., Francisco Rivera, A., Lee, L., Berroya, A., Vince Cruz, M., & Casintahen, D. (2003). Tagum study II: Follow-up study at two years of age after prenatal exposure to mercury. Pediatrics, 111, 289-295.

Risher, J., Murray, E., & Prince, G. (2002) Organic mercury compounds: human exposure and its relevance to public health. Toxicology and Industrial Health, 18, 109-160.

United States Department of Health and Human Services (HHS) and United States Environmental Protection Agency (EPA) (2004). FDA and EPA announce the revised consumer advisory on methylmercury in fish. Available at: http://www.fda.gov/bbs/topics/news/2004/NEW0138.html

United States Environmental Protection Agency (EPA) (March 2006). Clean Air Markets-Allowance Trading. http://www.epa.gov/airmarkets/trading/basics/index.html. Retrieved 23 January 2007.

United States Environmental Protection Agency (EPA) (2001). Mercury update: impact on fish advisories 2001. U.S. EPA, 823, Fact Sheet F-01-011.

United States Geological Survey (USGS) (1995). Mercury contamination of Aquatic Ecosystems. U.S. Department of the Interior, Fact Sheet FS-216-95.

World Health Organization (WHO) (1991). Environmental health criteria for inorganic mercury. WHO, International Programme on Chemical Safety, 118.

Yasutake, a., Hirayama, K., & Inoue, M. (1990). Interaction of methylmercury compounds with albumin. Arch. Toxicol., 64, 639-643.